MOST COMMON FORMS OF EXTRARESPIRATORY TUBERCULOSIS IN THE PATIENTS WITH HIV-AIDS

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Abstract: We present the common forms of extrapulmonary tuberculosis in the patients with HIV-AIDS: peripheral lymph nodes tuberculosis, peritoneal tuberculosis, tuberculous pericarditis, tuberculous meningitis.

Cuvinte cheie: tuberculoză extrarespiratorie, HIV, SIDA Rezumat: Articolul prezintă câteva din cele mai frecvente forme de tuberculoză extrapulmonară la infectații HIV-SIDA: tuberculoza ganglionară periferică, pericardita bacilară, peritonita bacilară, meningita bacilară.

TB is a pandemic global disease, more than 2 billion people, representing one third of the world population are infected with TB bacillus. One in ten people infected with Mycobacterium tuberculosis will manifest the disease during their life; the people infected with HIV present a higher risk.

Once infected with Mycobacterium tuberculosis, coinfection with HIV is the most important risk factor for the activation of latent tuberculosis.

The outbreak of tuberculosis in HIV positive patients in the early 90s was characterized by rapid development, increased number of cases, severity of the clinical forms, increased mortality and number of cases resistant to therapy. Given the impact of HIV on TB recrudescence since 1993 in the US, reporting new cases of tuberculosis includes case data of HIV patients. This is the recommendation of the National Tuberculosis Control Programme 2007-2011, all TB patients to be compulsorily tested for HIV.

Tuberculosis can affect any organ or tissue in the body, the disease can also have extrapulmonary sites. The classic definition of extrapulmonary tuberculosis is the tuberculous involvement of an organ other than the lung. However, when an extrapulmonary location is evident in a patient with pulmonary tuberculosis, these patients are under observation in pulmonary tuberculosis group.

The extrarespiratory origin of tuberculosis outbreaks are usually developed during metastatic hematogenous primary infection. These outbreaks may develop early, before the primary infection heals, towards phenomena of latent illness or at distance from the first infection by reactivating the lesions healed. In this study, we outlined some of the general features of the extrarespiratory tuberculosis:

- Symptoms, less familiar to physicians as locations, often inaccessible to investigations which often delay the diagnosis;
- Ø the discovery of a localization makes full attention to be focused on that outbreak, sometimes neglecting the possibility of other co-locations;
- the small number of bacilli in extrarespiratory locations makes bacteriological confirmation difficult and often

requires invasive diagnostic means.

HIV should always be suspected in cases of extrarespiratory tuberculosis given the frequent association of both diseases.

In the past, extrapulmonary tuberculosis was a common childhood disease, decreasing with age and again culminating in elderly people. In the post-AIDS period, tuberculosis with multiple determinations is prevalent in the people with immune deficiency. Extrapulmonary tuberculosis has become more frequent with the possibility of HIV infection occurrence, and on the other hand, has become a significant cause of morbidity and mortality in HIV positive patients (Table no. 1).

Table no. 1. Distribution of TB cases of according to site in HIV infected patients

SITE	TBEP SITE	%
Only TBCP (30%)		
Only TBCEP (20%) or both (50%)	TBCGg	35%
	TB pleuresy	20%
	Other	45%

Legend: TBCP-pulmonary tuberculosis, TBCEP - extrapulmonary tuberculosis, TBCGg-node tuberculosis

The risk of extrapulmonary tuberculosis and microbacteremia increases with advancing of immunosuppression. The low number of CD4 cells is associated with a greater likelihood of extrapulmonary disease in the patients with AIDS.

Those with the average CD4 count of $350~\text{mm}^3$ have been reported with lung disease, those with average $250~\text{mm}^3$ localized extrapulmonary tuberculosis, those with $140~\text{mm}^3$ with meningitis and those with $70~\text{mm}^3$ with bacteremia (Dube and colab.,1992).

The clinical signs and symptoms indicating any suspicion of extrapulmonary tuberculosis are presented in table no. 2.

The most common extrarespiratory sites of tuberculosis in infected HIV patients occur in advanced stages

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of immunosuppression and are:

- Ø peripheral lymph nodes tuberculosis
- Ø serous tuberculosis (ascites, pericardial)
- Ø tuberculous meningitis

The following briefly presents the most common forms of extrarespiratory tuberculosis in HIV infected patients.

Table no. 2. Clinical signs pointing out extrapulmonary tuberculosis

Ascites with lymphocyte predominance and negative cultures
Chronic lymphadenopathy (especially cervical)

CSF with predominance of lymphocytes, high protein and low

The differential diagnosis of Crohn's disease and ameobiasis

Pleural effusion with predominance of lymphocytes, bacterial cultures and pleural thickening

HIV Infections

Monoarticulary inflammation with negative cultures

Persistent sterile pyuria

TB endemic country of origin

Pericardial effusion, constrictive pericarditis or pericardial calcifications unexplained

Vertebral osteomyelitis of thoracic spine

Peripheral lymph nodes tuberculosis

Peripheral lymph nodes tuberculosis is the most common extrarespiratory location of tuberculosis. The most affected group is the laterocervical and submandibular nodes. The association with HIV causes simultaneous damage to both intrathoracic and extrathoracic lymph nodes. Clinically, the lymphs are swollen, painless, and can make fistulae with slow healing. Bacteriological or histopathological diagnosis is fistular exudate or lymph node biopsy examination of the product which may be positive in 25-50% of cases. The differential diagnosis is made with other nonspecific lymphadenitis.

Peritoneal tuberculosis

Peritoneal tuberculosis is present in two clinical forms: chronic adhesive peritonitis evolving with loss of appetite, weight deficit, low grade fever, abdominal masses and ascitic peritonitis (painless), representing the most common form. Exudative ascites fluid is more than 5% protein and 50 to 10,000 leukocytes/mm³, most lymphocytes. Bk smear is rarely positive, and cultures were positive in 50% of cases. Fever and ascites may suggest peritoneal tuberculosis. For a positive diagnosis, peritoneal puncture biopsy can be performed, as well as cytochemical examination and bacteriology of the fluid, or laparoscopy.

Tuberculous pericarditis

The most common form of tuberculous pericarditis is characterized by thickening of the pericardium, covering the epicardium and the presence of exudate. Pericardial exudate is the result of hypersensitivity reactions, the bacillus being rarely identified, the exudates is not purulent and the response to the antituberculosis treatment is often prompt. In certain cases, pericardium can accommodate large amounts of fluid and may compromise the hemodynamics. The exudate is sero-sanghinolent with 500-50000 elements/mm³ with lymphocytes predominance. In 25-35% of cases, smear and culture are positive. The absence of bacteriological and histological confirmation does not exclude pericardial tuberculosis.

Tuberculous meningitis

In Romania, in 2010, there were 129 cases of

meningo-encephalitis and four TB cases of the NCS - other than meningo-encephalitis (tuberculom).

The diagnosis of tuberculous meningitis is the presence of the meningeal clinical syndrome and based on the examination of the cerebrospinal fluid obtained by spinal puncture. Clinically, the patient has fever, headache, vomiting, constipation, skin hyperesthesia, photophobia, bradycardia, signs of Kernig I and II, positive Brudzinski, stiff neck, paralysis of cranial nerves.

Spinal fluid is clear, slightly hypertensive; biochemically it has a high level of protein (over 40mg/dl), forming an opalescent film in LRC kept in the refrigerator, low level of glucose (below 50mg/dl), lower than 700 mg/dl chlorides, few cellular elements, several hundred/mm³, commonly lymphocytes. Bacteriologically, the microscopic examination identified only 25% bacilli in veil, the culture media for Bk adds the bacteriological confirmation up to 75%.

Fundus examination shows the presence of choroidal tubercles, two 2UI PPD tuberculin test is frequently positive in 2/3 of cases. Tuberculous meningitis occurring in HIV patients can be considered after eliminating the criptococcus etiology.

The severity of extrarespiratory tuberculosis is due on one hand on the frequency of late diagnosis on the other hand, on the complicated evolution of the disease, if the treatment is started too late. It is essential that clinicians know about the extrapulmonary manifestations of tuberculosis, so that disease, which is otherwise curable, to be recognized and treated, the patients infected with HIV – AIDS and tuberculosis, requiring an interdisciplinary approach.

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